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Scale-up of membrane affinity adsorbers based on tested physical model

S. Dimartino[1,2], C. Boi*[1], G.C. Sarti[1]

[1]University of Bologna, Italy, [2]University of Christchurch, New Zealand

Membrane chromatography represents one of the emerging technologies for downstream processing in the biotechnology industry. This process is currently used in polishing steps for antibody manufacturing, while its application it is still uncommon for the capturing step. To promote its application in large scale processes, it is imperative to develop a reliable simulation tool able to describe the process performance at all scales in a predictive way.

This work presents a mathematical model for the description of protein purification with affinity membranes. The model proposed describes all the three stages of the chromatographic cycle and takes into account convection, axial dispersion and binding reaction kinetics in the porous membrane matrix, while boundary layer mass transfer resistance is shown to be negligible [1]. The model also considers the extra column contributions to band spreading due to dead end volumes and mixing effects. All model parameters have a precise physical meaning which enables their evaluation through separate experimental measurements, independent of the chromatographic cycle.

Model testing and validation is achieved by comparing simulation results with an extensive set of experimental data obtained for chromatographic cycles using different affinity membranes; the experimental system considered is the primary capture of IgG1 from a cell culture supernatant. A detailed analysis of the experimental data indicates that a bi-Langmuir binding kinetics is essential for a correct process description up to the saturation of the stationary phase [2].

The comparison between model calculations and experimental data shows good agreement for all stages of the affinity cycle. In particular, for loading and washing steps, binding kinetics is found so fast that adsorption equilibrium is sufficient to describe the observed behaviour; as a result, the model simulations are entirely predictive for the adsorption and washing phases. On the contrary, in the elution step the reaction rate is comparable to that of the other simultaneous transport phenomena. Remarkably, the model is able to predict the performance of chromatographic purification of IgG from complex mixtures simply on the basis of the parameter values obtained from pure IgG solutions.

The good agreement of the model predictions with experimental data for the different supports considered demonstrates the model accuracy for the description of all the relevant transport mechanisms involved.

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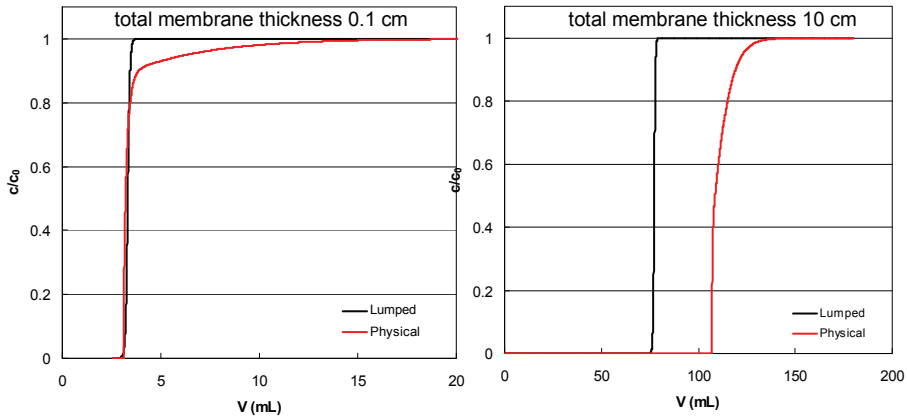

Figure 1. Comparison between lumped and physical model: lab scale, 0.1 cm thickness (left) and scapeup configuration, 10 cm thickness (right).

The model has been finally applied for different scale-up calculations for membrane adsorbers, varying area and column thickness. The results have been compared with a simpler and frequently used lumped model; interestingly, both models which can describe equally well the lab scale process, but on the contrary they lead to important differences in the scale-up calculations, for which the physically based model is indeed more reliable.

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